

## REMARKS

Claims 1-56 are pending in the present application. Claims 1, 15 and 25 have been amended to recite that the methods are performed *in vitro*. Support for this amendment may be found throughout the specification, particularly in Examples 1 and 2. Therefore, these amendments do not add new matter, and their entry is respectfully requested.

### Rejection Under 35 U.S.C. § 102(b)

Claims 1-5, 8-10, 12-14, 25, 26, 28-31, 37-41, 44, 45 and 49-54 were rejected as being anticipated by Shuman (US 5,766,891). This rejection is respectfully traversed.

Shuman is cited as teaching a method of generating a double stranded recombinant nucleic acid by contacting a first ds nucleotide sequence, a second ds nucleotide sequence, and a topoisomerase such that the topoisomerase covalently link both strands of the first sequence to the second sequence generating a ds recombinant molecule.

As discussed in the previous response filed December 16, 2004, the present claims recite that the topoisomerase covalently links both strands of at least one end of the first ds nucleotide sequence to both strands of at least one end of the second ds nucleotide sequence to obtain a recombinant ds nucleic acid molecule that "does not contain a nick in either strand at the position where the ds nucleotide sequences are joined." In contrast, the method of Shuman results in a recombinant molecule containing a nick where the two sequences were joined. As such, the claimed invention is distinguishable from Shuman in that, according to the present methods,

topoisomerase covalently links both strands of two nucleotide sequences at the position where the sequences are joined.

Although Applicants maintain that the claims as amended in the response filed December 16, 2004, distinguish the present invention from Shuman, the claims have been amended herein to recite that the methods are performed *in vitro* in order to expedite prosecution of the application. The present claims recite that the ds nucleic acid sequences and topoisomerase are contacted *in vitro* to produce a ds recombinant nucleic acid molecule which does not contain a nick in either strand at the position where the ds nucleotide sequences are joined. Shuman does not teach this feature. Thus, the claims are not anticipated by this reference.

In view of the amendments and comments discussed above, applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102(b).

***Rejections Under 35 U.S.C. § 103 (a)***

1. Claims 32-34 and 36 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over Shuman (US 5,766,891). This rejection is respectfully traversed.

Shuman is applied for the reasons set forth above. It is acknowledged in the Office Action that Shuman does not teach using a third ds nucleotide sequence, but alleged that the skilled artisan would have been motivated to further bind a third ds nucleotide sequence to generate a desired construct. As discussed above, Shuman does not teach an *in vitro* recombination method which results in a recombinant DNA molecule which does not contain a

nick in either strand at the positions where the ds nucleotide sequences are joined. In addition, Shuman does not suggest such an *in vitro* recombination method. Accordingly, the claimed invention would not have been obvious in view of Shuman, and it is therefore respectfully requested that the rejection of claims 32 to 34 and 36 be removed.

2. Claims 6, 7, 11, 15 to 24, 27 and 35 were rejected under 35 U.S.C. § 103(a) as being obvious over Shuman in view of Yarovsky. Applicants respectfully traverse this rejection.

The Office Action alleges that the skilled artisan would have been motivated to apply Yarovsky's topoisomerase adapted vectors to the method of Shuman in order to bind amplified sequences into vectors.

Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Specifically, establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and/or knowledge available to one of skill in the art would have lead that individual to arrive at the claimed invention. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Moreover, establishing *prima facie* obviousness requires not only a showing that such a combination of prior art teachings is possible, but also that the teachings would have 1) motivated the skilled artisan to make the combination to arrive at the claimed invention, and 2) suggested to the skilled artisan a reasonable likelihood of success in making and using the claimed invention. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988).

Absent a showing of such motivation and suggestion, *prima facie* obviousness is not established.

*See Fine*, 5 USPQ2d at 1598.

As discussed above, Shuman does not teach an *in vitro* method in which the resulting ds recombinant nucleic acid molecule does not contain a nick in either strand at the position where the ds nucleotide sequences are joined. Yarovsky does not cure this defect in the teaching of Shuman. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

3. Claims 42 and 43 were under 35 U.S.C. § 103(a) as being obvious over Shuman in view of Seed et al. Applicants respectfully traverse this rejection.

The Office Action contends that one of ordinary skill in the art would have been motivated to apply Shuman's method of construction to express the T7 suppressor gene of Seed et al. in order to express and produce T7 suppressor, which can be used for diagnostic and therapeutic purposes.

As discussed above, Shuman does not teach an *in vitro* method in which the resulting ds recombinant nucleic acid molecule does not contain a nick in either strand at the position where the ds nucleotide sequences are joined. Seed et al. do not cure this defect in the teaching of Shuman. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

4. Claims 46 to 48 were rejected under 35 U.S.C. § 103(a) as being obvious over Shuman in view of Trono et al. Applicants respectfully traverse this rejection.

The Office Action alleges that one of ordinary skill in the art would have been motivated to apply the teaching of a histidine tag by Trono et al. to an expression system as described by Shuman in order to purify an expressed protein.

As discussed above, Shuman does not teach an *in vitro* method in which the resulting ds recombinant nucleic acid molecule does not contain a nick in either strand at the position where the ds nucleotide sequences are joined. Trono does not cure this defect in the teaching of Shuman. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

In summary, none of these references, either alone or in combination, teach or suggest an *in vitro* method in which the resulting ds recombinant nucleic acid molecule does not contain a nick in either strand at the position where the ds nucleotide sequences are joined. Because the independent claims are novel and non-obvious, the dependent claims are necessarily novel and non-obvious.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Commissioner is authorized to charge Deposit Account No. 07-1896 if any fee is deemed necessary.

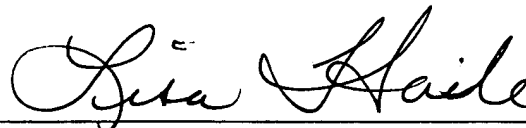
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The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Respectfully submitted,

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